MERIDIAN
MEDICAL TECHNOLOGIES®
A Pfizer Company

Meridian Medical Technologies®, Inc.
1945 Craig Road
St. Louis, MO 63146

January 31, 2018

Miguel A. Hernández
Director, Compliance Branch
US Food and Drug Administration
8050 Marshall Drive, Suite 205
Lenexa, KS 66214

RE: Meridian Medical Technologies, Inc. / FEI Number: 1950222
Quarterly Action Plan Update for 4th Quarter 2017 – Inspection Response Status

Dear Mr. Hernández:

In the April 14, 2017 response to the U.S Food and Drug Administration ("FDA") Form 483 issued March 24, 2017, Meridian Medical Technologies, Inc., a Pfizer company ("MMT") committed to provide FDA with Quarterly Updates with respect to its 483 response commitments. Also in the response, MMT committed to working with a third party GMP consultant to develop a Compliance Action Plan ("CAP") which would ensure a holistic response to the 483 observations as well as the broader GMP subsystems related to the Observations (Exhibit 1). The CAP is an iterative document and is updated as action items are completed or if internal assessment work completed as part of the CAP directly indicates additional compliance commitments.

After receiving the FDA Warning Letter on September 05, 2017, MMT made additional commitments in the September 26, 2017 Warning Letter Response regarding specific deliverables that would be communicated to FDA via these quarterly updates. The Warning Letter Response commitments are also added to the CAP. Additionally, there were specific commitments made to FDA during our FDA/MMT Joint Regulatory Meeting on November 09, 2017, which are now included in the CAP.

The CAP reports the status of commitments for the fourth quarter of 2017 as of December 31, 2017.

MMT's Progress

During the fourth quarter, MMT completed a number of significant actions, including the following:

- A new leadership role was created within the Quality Operations organization, Combination Product Program Director, to oversee combination product quality and compliance, including Design Controls. A colleague from Pfizer Global Supply (PGS), who is an engineer and Subject Matter Expert in combination products, has filled this role in the interim since October 2017 and was present at the November 09, 2017 Regulatory Meeting with FDA. Active recruitment is in progress to fill this role.
- MMT implemented Design Control System Life Cycle (SLC) Within the Quality Management System
- MMT Engaged (b) (4) to conduct batch record review of all EpiPen batches, which includes the review of associated investigations as of November 2017. As previously communicated, MMT third party review will be (b) (4) (b) (4)

As committed in its Warning Letter Response, MMT has also completed the following two retrospective reviews:

- The retrospective assessment of complaints received September 08, 2015, through September 07, 2017, has been completed. This assessment confirmed that the previous prioritization of the complaint (normal, high, or expedite) did not have an impact on the outcome of the complaint investigation. Of the 450 quality complaints assessed under protocol, four met the criteria outlined in the protocol for escalation to above site senior leadership for additional review. Although some of these four complaint reports were found to need additional information within the complaint investigation document, the MMT subject matter experts were able to provide additional information (retain sample results, complaint sample evaluation results, and explanation of use of previously completed investigation) demonstrating that the investigations adequately assured the product units in the complaint were not defective and no market action is indicated. In each case, the potential for patient impact is low. The four specific investigations that were escalated have been updated to reflect the additional supporting details noted in the summary report. A summary report of this retrospective review is attached as Exhibit 2.
    - During the retrospective assessment of complaints, 144 of the 450 complaints did not have a valid lot number or no lot number could be obtained from the complainant. At the time of complaint receipt of the 144 complaints, complaints without lot numbers did not require investigation and during execution of the protocol, no investigation was assessed. A separate assessment was completed for these 144 complaints.

The complainant narrative, complaint class/subclass classification, and prioritization were assessed. A complaint can be received where multiple sub-classifications match the description of the narrative, the most appropriate sub-class is chosen based on root cause of subsequent defects (i.e. "Spontaneous Activation" instead of "Lack of Effect" – where the pen spontaneously activated resulting in lack of effect in patient narrative). Fourteen complaint sub-classifications could have been classified with a more appropriate classification corresponding to the narrative. MMT will update the complaints with the more appropriate classifications. The change in the classification had no impact on the current prioritization of the complaint. MMT procedures require an investigation for all complaints, whether or not a lot number is obtained from the complainant.

- The retrospective review of manufacturing investigations for the non EpiPen products manufactured at the site, ATNAA/DuoDote, Diazepam,(b) (4), and Pralidoxime Chloride, was also completed. This review resulted in 374 total investigations being reviewed in detail under protocol, with a resulting 13 of these investigations meeting protocol criteria that required escalation of the investigation for above site senior leadership review. The conclusion of this review was that the escalated investigations were performed in alignment with SOPs, correct product impact and disposition decisions were made. The above site review also included evaluation and discussion of any concerns that would present undue risk to patients or require market actions. The review affirmed that there was no change to patient impact/risk as a result of any new information obtained through the retrospective review and original decisions were appropriate. A summary report of this retrospective review is attached as Exhibit 3.

- By the end of the 4th Quarter of 2017, MMT had completed 94% of the commitments in response to the 2017 483, and 45% of its commitments made in response to the Warning Letter. MMT is also tracking actions identified in the course of its regulatory commitments in the CAP and 29% of the 120 commitments have been completed, see Exhibit 4 for CAP dashboard. One 483 commitment was not completed by the targeted date in the 4th quarter. MMT had committed in the 483 response to complete the revalidation of the EpiPen process end to end. The revalidation was targeted to be completed by December 15, 2017 based on the plan to implement the changes during Fall Aseptic shutdown planned for September 2017. To minimize stock-outs of military products and potential stock-outs of EpiPen products, the Fall Aseptic shutdown was postponed to mid-October 2017 with resumption of operations planned for the end of November 2017. Initiation of process validation (PV) after initiation of the media fill activities associated with improvements made to the (b) (4) Filler commenced on December 11, 2017. To date all PV batches have been formulated and filled. Completion

of the PV lot final validation report is now anticipated to be on or before February 28, 2018.

Completion of evaluation of literature and real world databases regarding usage rates

As discussed at the Regulatory Meeting between FDA and MMT/Pfizer on November 9, 2017, MMT undertook a review of literature and real world databases to determine an estimated usage rate for EpiPen auto-injectors. While there are limitations in the studies described in the literature and in the real world databases, these available data sources provide information which permit an estimate of the usage rate for the product. Based on MMT's analyses of available literature and pharmaceutical claims data set, the estimate usage rate of 5% annually for EpiPen auto-injectors is considered representative of the annual usage rate and is recommended for use in analyses (Exhibit 5).

Effectiveness Checks at MMT

Pfizer has recently engaged (b) (4) to provide effectiveness check of CAPAs from regulatory commitments relating to the March 2017 483, and the 2017 Warning Letter, as well as the actions implemented in response to the site's ongoing remediation efforts. The first site visit by (b) (4) is scheduled to begin February 2018.

Commitment to Continued Communication with FDA

MMT will continue to submit updates on CAPA status, with the next Quarterly Update to be submitted on or before April 30, 2018. In the short-term, Pfizer corporate and site management are available at your request to address any further issues you may wish to discuss. As discussed at the November 09, 2017 Regulatory Meeting, Pfizer welcomes the opportunity to discuss with you our progress. John Kelly will also be in touch with Francis Godwin to determine need for a meeting.

Please note that this letter and the corresponding attachments contain confidential information related to MMT's business operations and processes and accordingly are not subject to disclosure under the Freedom of Information Act, 5 USC 552(b)(4) and 21 C.F.R 20.61(a)-(b).

Sincerely,

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cc: Cheryl Bigham, District Director, Kansas City District Office
Francis Godwin, Director (Acting), Office of Manufacturing Quality (OMQ), CDER/OC
John F. Kelly, VP, Quality Operations and EHS, Pfizer
Thomas Handel, General Manager, MMT

Exhibit 1: Compliance Action Plan (CAP) – (approved 30Jun2017) with Most Current CAP Appendix I (last updated 31Dec2017)

Exhibit 2: Quality Retrospective Complaint Assessment of Product Quality Complaints for EpiPen – Summary Report

Exhibit 3: Retrospective non-Epinephrine Auto-Injector Manufacturing Investigation Review Summary Report

Exhibit 4: Compliance Action Plan (CAP) dashboard (last updated December 31, 2017)

Exhibit 5: EpiPen Usage Rate Estimate Report, EpiPen NGA Auto-Injector

Exhibit 1. Compliance Action Plan (CAP) – (approved 30Jun2017) with Most Current CAP Appendix I (last updated 31DEC2017)

Compliance Action Plan (CAP)

for:

Meridian Medical Technologies, Inc.
St. Louis, MO

June 29, 2017

Prepared By / Date:

Jeff A. Schramer 29 Jun 2017

Jeffrey A. Schramer
Site Quality Leader, MMT

Approved By / Date:

29 JUNE 2017

Tom Handel
President and General Manager, MMT

Approved By / Date:

(1)

Kevin Jenkins
Vice President of Quality Excellence, Pfizer Corporation

(1) See signed cover page of emailed scan. Scan signed by K. Jenkins on 30 Jun 2017. JA. Schramer 26 Jul 2017

Compliance Action Plan (CAP)

for:

Meridian Medical Technologies, Inc.
St. Louis, MO

June 29, 2017

Prepared By / Date:
Jeffrey A. Schramer, 29 Jun 2017
Jeffrey A. Schramer
Site Quality Leader, MMT

Approved By / Date:
29 June 2017
Tom Handel
President and General Manager, MMT

Approved By / Date:
30 June 2017
Kevin Jenkins
Vice President of Quality Excellence, Pfizer Corporation

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1. INTRODUCTION

Meridian Medical Technologies, Inc., a Pfizer Company (hereafter MMT) located at St Louis, MO, was inspected by the U.S. Food and Drug Administration (FDA) from February 20 through March 24, 2017. At the conclusion of the Agency's inspection on March 24, 2017, MMT received a Form 483 with 14 multi-part observations relating to the manufacture of the firm's auto-injector combination products.

MMT submitted a written response to the Form 483 on April 14, 2017. Within the response was a commitment to engage a third party consultant that specializes in Quality System Remediation. To that end, (b) (4) was retained by MMT as the identified 3rd party in May 2017. Specifically, (b) (4) involvement was to review and provide input to this document, to conduct in-depth audits of the three (3) priority topics listed directly below in the next paragraph, and to identify the topics/areas listed under Section 5 that are in need of a rigorous audit, in order to establish the level of compliance.

One of the deliverables within the 483 Response, was for MMT to create a Compliance Action Plan (CAP). It was communicated within our 483 response that the CAP would focus on three key areas for assessment by the 3rd party, which would then result in corresponding improvement commitments by MMT. The following systems communicated to be further assessed by a 3rd party are:

- Design Controls
- Complaint Investigations
- AQLs (Sampling Plans)

Furthermore, the 483 Response stated the CAP would include any new commitments that arise from gap assessments/reviews performed as part of the 483 response commitments, as well as any additional quality systems requested for evaluation by a 3rd party consultant.

2. PURPOSE

The CAP is intended to document corrective and preventive actions arising from assessment work described above, in addition to the commitments previously provided in MMT's original April 14, 2017 483 Response. This CAP supplements the Form 483 response and provides assurance that a comprehensive, holistic approach is being taken by MMT. The CAP will also be utilized to document corrective and preventative action effectiveness checks (which will be conducted by a 3rd party) for all commitments within the CAP.

The in depth 3rd party assessments of existing systems and CAPA effectiveness verification work will follow completion of the initial version of this CAP. CAP Appendix I will be updated on (b) (4) basis to provide tracking information to the

compliance initiatives stated within the CAP and each update will be approved by management.

3. GOVERNANCE AND OVERSIGHT

In order to provide focused resources for manufacturing sites undergoing remediation, Pfizer established a Quality Excellence Team (QET) to provide focus and support on improvement at sites undergoing remediation in May 2017. The QET is co-led by Operations and Quality, with dual reporting to the VP Pharmaceutical Manufacturing Operations and the VP Quality Operations and Environmental Health & Safety and accountability to Pfizer's Leadership Team Governance as described below.

The objective of the QET is to deliver a focused and aligned approach to development and execution of quality improvement activities at selected network sites in order to achieve/maintain Voluntary Action Indicated (VAI) status. The team's responsibilities include the following:

- Ensuring comprehensive quality improvement plans for each site in scope are in place and incorporate actions and recommendations from regulatory inspections and internal/external assessments
- Providing above site project management, as well as frequent updates to sponsors
- Ensuring projects are prioritized and resourced appropriately and programs/training are developed as needed
- Accelerating key projects and driving overall timelines, ensuring regulatory commitments are made
- And ensuring consistency for specific improvements applicable across multiple sites.

The integration of the CAP deliverables into the QET Oversight and Governance process are further described in the Communication section of this document.

Below is the governance structure of the QET:

4. APPROACH AND METHODOLOGY

Development of this CAP included (b) (4) review of the Form 483 observations, MMT's responses, physical inspection/tours of buildings and facilities, performing reviews of records and procedures, and conducting interviews with MMT management and key staff personnel.

5. CAP SCOPE AND TIMING

As described in the FDA response commitment letter, MMT previously identified three key areas for improvement that will be a primary focus of the 3rd party assessments required for the CAP, namely:

- Design Controls
- Complaint Investigations
- AQLs (Sampling Plans)

Additionally, other areas / topics for evaluation were identified by either MMT or (b) (4) through staff interviews, document reviews and facility tours that were conducted by (b) (4) during the weeks of May 15, May 22, and June 5, 2017. A tiered risk-ranking was performed for all the topics identified. Risk was predicated on potential impact to patient safety, product quality, pre-existing internal assessments/improvement plans, and/or regulatory compliance. Other factors

considered with respect to risk were: whether the issues identified by FDA and MMT's proposed corrective actions appeared to have a comprehensive approach toward resolution as described in the MMT 483 response (per (b) (4) evaluation of MMT's 483 response), whether the issues within the FDA 483 were one-off occurrences vs. systemic cause; or other factors that suggested a comprehensive evaluation was warranted. The priorities for the comprehensive evaluations to be conducted by the 3rd party are below, and separated into two phases. (b) (4) (b) (4) Below are the quality systems and timelines expected for PHASE I and PHASE II:

PHASE I (b) (4) **Assessments of the PHASE I topics below are expected to be completed by July 15, 2017, and the corresponding MMT CAPAs to be identified by July 30, 2017)**

(b) (4)

PHASE II (3rd Party Consultant Assessments to be completed by October 1, 2017, and the corresponding MMT CAPAs to be identified by October 31, 2017)

(b) (4)

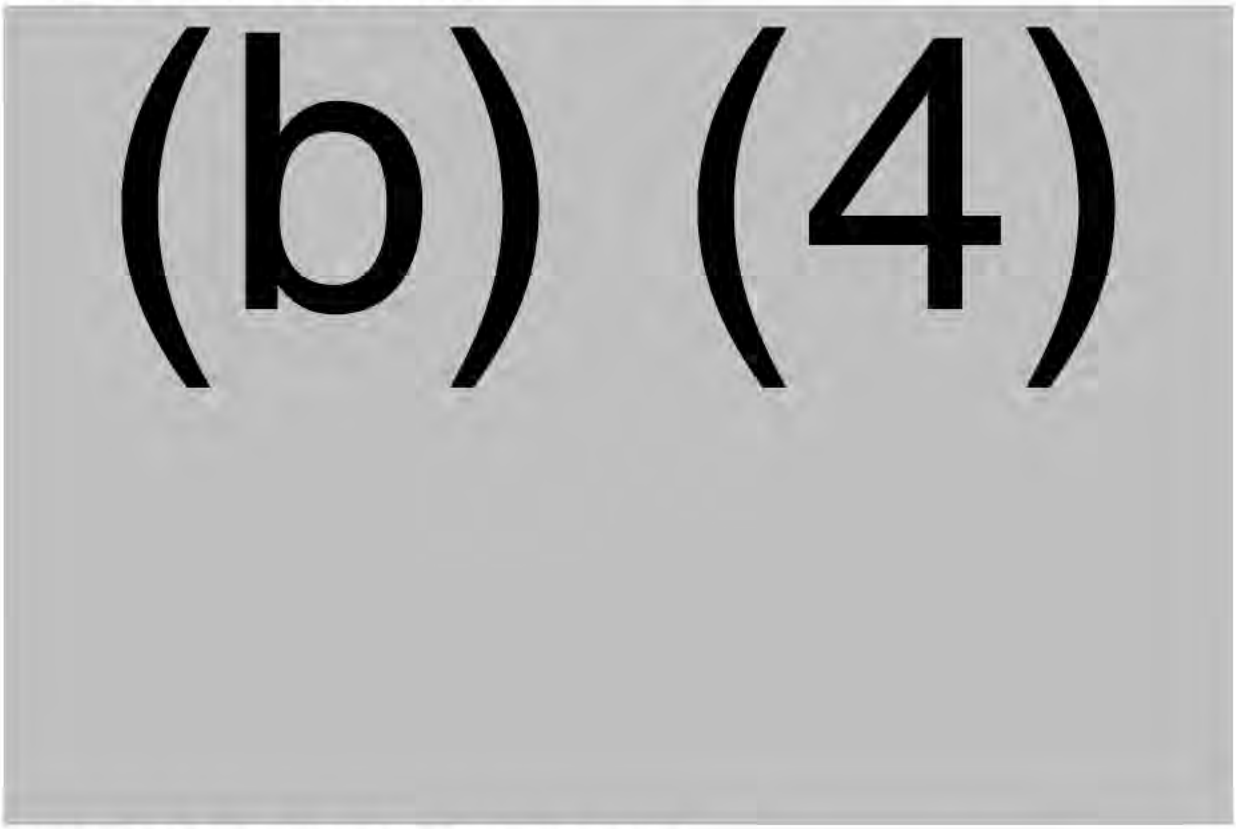
6. PROJECT OVERVIEW

The objectives of this CAP will be achieved by completion of the following key steps:

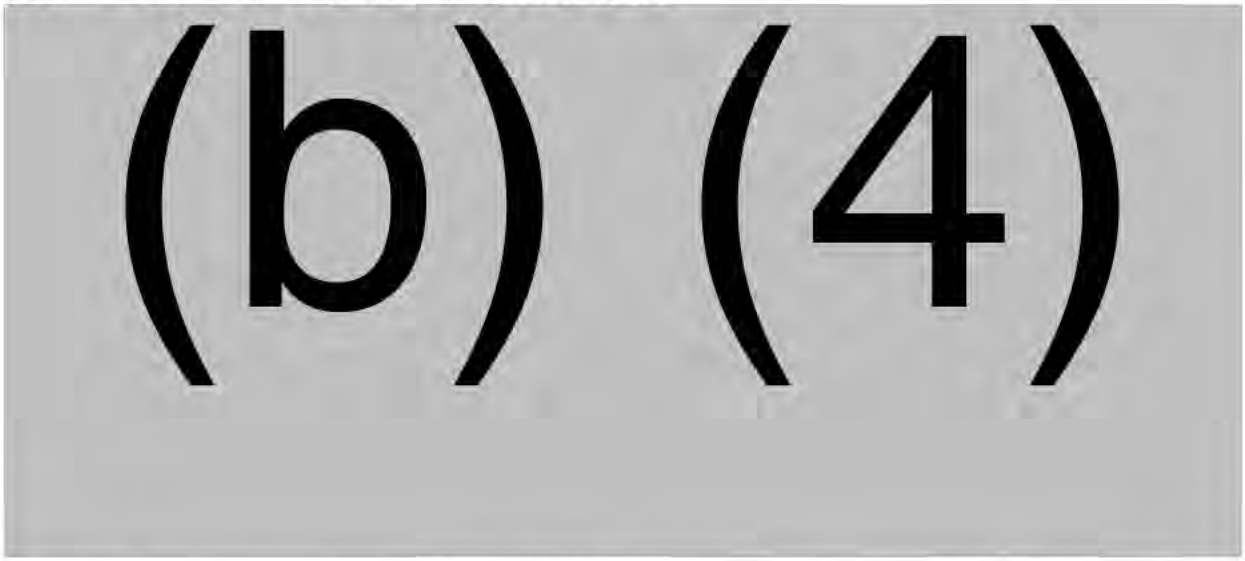
(b) (4)

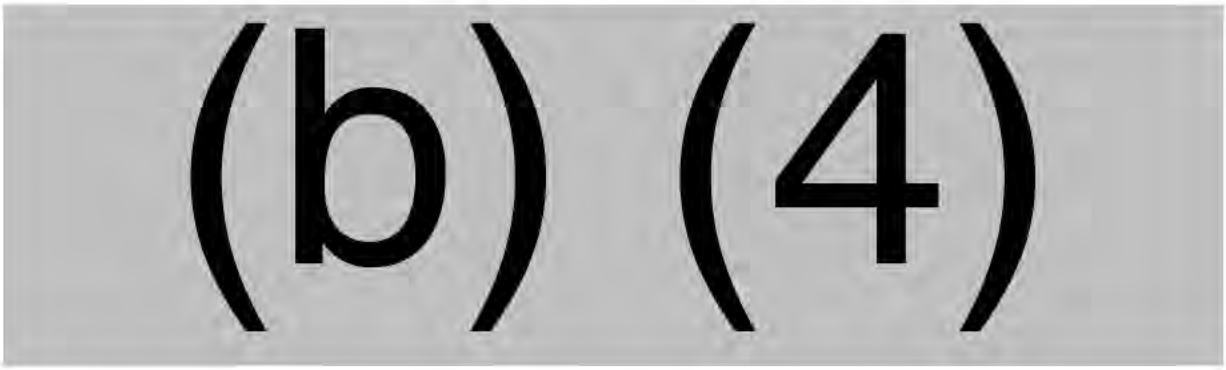
7. THIRD PARTY AUDIT DETAILS

A more detailed description of the comprehensive 3rd party evaluations described within Section 5 Phase I and II is as follows:



8. CORRECTIVE AND PREVENTATIVE ACTIONS





9. COMMUNICATION

A Steering Committee comprised of leadership with executive responsibility for MMT and QET Leads will meet (b) (4) to discuss progress on the Compliance Action Plan.

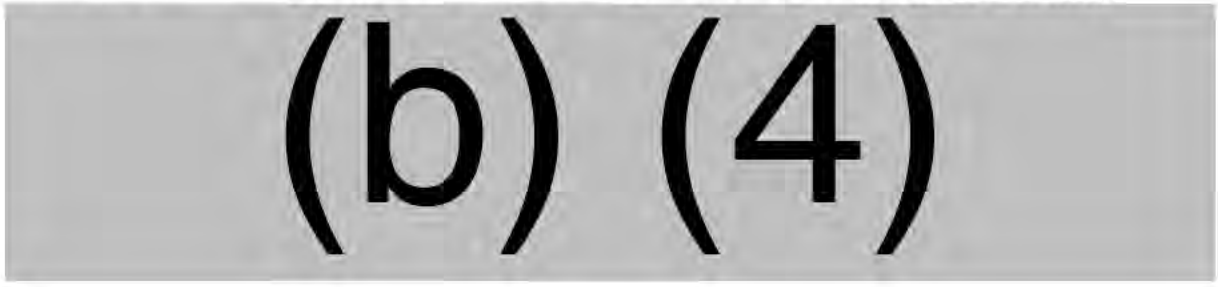
Standing agenda for the (b) (4) meetings are to include:

- Action Items
- CAPA Commitment Dashboard
- (b) (4) Snapshot (recently completed activity and look ahead to the coming actions)
- Staffing Update
- Discussion Items
- Any specific commitment detail that needs Governance visibility/alignment
- Routine Quality Performance - Investigation Status

The CAP APPENDIX I will be updated on a (b) (4) The CAP and the newly updated APPENDIX I will be provided to the FDA within one month following the (b) (4) update of APPENDIX I, until such time that all 483 Response and CAP related CAPA are completed along with successful effectiveness checks.

10. CRITERIA FOR SUCCESS:

Criteria for determining project success include, but are not limited to, the following:



APPENDIX I
Compliance Action Plan Related CAPA Status
(Version **4.0** Updated Date – **as of December 31, 2017**)

APPENDIX I Update Prepared By / Date:

Nicole Typaldos 23JAN2018

Nicole Typaldos
Quality Systems Manager, MMT

APPENDIX I Approval By / Date:

Jeffrey A. Schramer 31 Jan 2018

Jeffrey A. Schramer
Site Quality Operations Leader, MMT

Table I **Third Party Assessment Tracking**

(b) (4)

Table II FDA 483 Related Corrective and Preventative Action Tracking, by order of Observation and Due Date

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Cover Letter	MMT will engage SME's within the Pfizer / Meridian / Industry network and experienced independent consultants with significant experience with medical device quality systems to develop a Compliance Action Plan (CAP) that will identify corrective and preventative actions that will enhance our systems and processes. The CAP will focus on three primary areas for improvement, as identified in the observations and out own internal discussions: Design controls (including DHF) Complaint Investigations Acceptable Quality Limits (AQL)	15-Jun-17	15-Jun-17	Quality Systems		
FDA Inspection	Cover Letter	Submit updates to FDA on a quarterly basis, with the first update to be submitted by July 30, 2017 (for the three month period ending June 30, 2017). First Update will include a copy of our CAP.	30-Jul-17	30-Jul-17	Quality Systems		
FDA Inspection	1, 4, 6, 8	Update the standard sampling plan for EpiPen finished good functionality test to (b) (4) units (b) (4) , (b) (4) AQL from (b) (4) to (b) (4) The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) AQL of (b) (4) final product functionality testing. The current AQL of (b) (4) sampling plan (for critical defects) will be modified to (b) (4) AQL of (b) (4) for product release testing. (See Response 6A table 4) The current AQL of (b) (4) sampling plan (for critical defects) will be modified to yield a (b) (4) AQL of (b) (4) for product release testing. (See Response 6A table 4) (b) (4) AQL applied for release testing will be instituted For those essential functional attributes as design inputs and outputs are confirmed critical through risk assessment process, a (b) (4) specification with a (b) (4) AQL for determination of sample size will be applied for release testing reflecting system level reliability.	30-Apr-17	28-Apr-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	1, 13	SOP-QLA-MQA-00720 to be updated to assure consistent application across lots in the scope of an investigation when additional testing is performed to evaluate potential quality impact SOP-QLA-MQA-00720 will be revised to require that all on-going preventative actions that address root cause are included in an investigation report SOP-QLA-MQA-00720 will be revised to require that deviation investigators implement the use of (b) (4) to identify when the item or event being investigated differs from historical process trend as an aid in the investigation process SOP-QLA-MQA-00720 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4), be considered during relevant investigations	31-May-17	30-May-17	Quality Systems		
FDA Inspection	1	Update SOP-QLA-MQA-00004 to ensure that formal notification to management occurs for any OOS result, whether it be for a finished product, in-process sample, or incoming component	31-May-17	30-May-17	Quality Systems		
FDA Inspection	2	SOP-MAN-INS-00029 will be updated to add specific requirements for the (b) (4) for all product lines	31-May-17	19-May-17	Packaging & Inspection		
FDA Inspection	2, 14	New Job Aid to be created which includes (b) (4) and further details for the steps performed during the (b) (4) New OJT training document will be developed and implemented for all colleagues that perform (b) (4). The new OJT will require review of the job aid, review of SOP-PRO-CLP-00005, and hands on training (New Job Aid to be created which includes (b) (4) and further details for the steps performed during the (b) (4)	07-Jun-17	02-Jun-17	Aseptic Operations		
FDA Inspection	2	MVI performance improvement: (b) (4)	30-Jun-17	23-Jun-17	Packaging & Inspection		
FDA Inspection	2	AQL sampling will be adjusted so that results of the sampling are (b) (4)	31-Jul-17	28-Jul-17	Packaging & Inspection		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	MVI performance improvement: (b) (4) Any improvement opportunities will be incorporated into a process continuous improvement plan	31-Aug-17	31-Aug-17	Packaging & Inspection		
FDA Inspection	2	(b) (4)	30-Nov-17	30-Nov-17	Packaging & Inspection		
FDA Inspection	3	Statistical Analysis with (b) (4) Based on the analysis, statistically based lot trend alert limits will be identified for complaint sub-classes.	15-May-17	15-May-17	Complaints		
FDA Inspection	3, 13	SOP-QLC-QLE-00702 will be revised to clarify that site personnel can and should take action to address any combination of complaints, no matter the number, that appears to signal a trend or issue and to establish the following expectations with respect to alert limits: - statistically based alert limits for the number of complaints of a similar nature for the same lot for all products and all complaint sub-classes - a requirement that lot trend alert limits are based on statistical analysis of historical complaint data - a requirement that the statistically based lot trend alert limits be reviewed at least annually SOP-QLC-QLE-00702 will be revised to include an instruction that the potential impact of reprocessing or atypical environmental conditions, such as (b) (4), be considered during relevant investigations	31-May-17	31-May-17	Complaints		
FDA Inspection	3	Pfizer corporate procedure GPB-QS1073 will be updated to clarify the purpose of the expedited complaint process. As part of the update, all complaint classifications associated with devices and combination products will be evaluated to ensure alignment to the requirements of the specific regulatory notifications described above. In addition, all complaint classifications associated with the products manufactured at MMT will also be evaluated to ensure that any product specific exceptions regarding prioritization are included in the update to GPB-QS1073.	30-Jun-17	30-Jun-17	Complaints		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	3	SOP-QLC-QLE-00702 will be updated to reflect the clarifications in GPB-QS1073 regarding the purpose for expediting complaints	15-Jul-17	15-Jul-17	Complaints		
FDA Inspection	3	Risk Assessment will be performed including Safety/Medical/Clinical, to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk assessment will also establish acceptable mean complaint rates and will be reviewed at a minimum of annually as part of the Annual Product Review	31-Jul-17	28-Jul-17	Complaints		
FDA Inspection	3	Engaging experienced independent consultants with significant experience with medical device quality systems to conduct an assessment of the MMT quality systems, including Complaint Management. Assessment	31-Aug-17	25-Jul-17	Quality Systems		
FDA Inspection	3	Creation of Action Plan with timeframe for corrective actions (from consultant assessment of Complaints)	30-Sep-17	29-Sep-17	Complaints		
FDA Inspection	4	New procedure to conduct (b) (4) has been drafted and will be approved. (SOP-QLA-GEN-11104)	15-May-17	15-May-17	Operational Excellence		
FDA Inspection	4	A detailed roll-out plan for (b) (4) will be approved by Manufacturing and Quality. The (b) (4) to be conducted under the scope of the new procedure will be for the filling equipment for (b) (4). (b) (4) .	30-May-17	30-May-17	Operational Excellence		
FDA Inspection	4	Procedure will be developed by Operational Excellence, Manufacturing, and Quality to require routine in-process trending for ATNAA and EpiPen and to assess performance variability A new procedure will be developed by MMT to require routine in-process data trending of critical parameters to assess performance variability for ATNAA and EpiPen	30-Jun-17	23-Jun-17	Operational Excellence		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	Risk assessment, including representatives from the Safety/Medical/Clinical groups to document essential attributes for intended use and their criticality.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews in the APRR.	30-Aug-17	29-Aug-17	Quality Systems		
FDA Inspection	4	In-process trending at the site will be in place for identified critical processing areas. A review of these trend reports will be incorporated into periodic reviews at SQRT.	30-Aug-17	28-Aug-17	Quality Systems		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA Filling)	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	(b) (4)	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	Updates to the Process Maps are also being developed for current the products currently being manufactured at the site, ATNAA, to identify process input variables that can be further evaluated to enhance process capability. (ATNAA P&I)	31-Aug-17	31-Aug-17	Operational Excellence		
FDA Inspection	4	For those essential characteristics that are confirmed in the risk assessment and defined as critical in Table 2 of Response 6A, there will be a plan implemented to conduct testing based on system level reliability.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	4	(b) (4) batch records	30-Sep-17	29-Sep-17	Packaging & Inspection		
FDA Inspection	4	(b) (4) batch records	30-Sep-17	29-Sep-17	Packaging & Inspection		
FDA Inspection	4	Trend reporting, including (b) (4), will be incorporated into periodic reviews at Site Quality Review Team (SQRT) meetings for continuous improvement	31-Oct-17	05-Sep-17	Quality Systems		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	4	Trend reporting, including (b) (4), will be incorporated in the Annual Product Records Review (APRR) for continuous improvement	31-Oct-17	19-Oct-17	Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated into periodic reviews of Site Quality Review Team.	28-Feb-18		Quality Systems		
FDA Inspection	4	As an outcome of the capability studies, Six-Sigma projects will be employed to reduce variability where improvement areas are identified. Results from the capability studies will be incorporated in the Annual Product Record Review (APRR).	28-Feb-18	19-Oct-17	Quality Systems		
FDA Inspection	5	Complaint trend reports will be based on (b) (4) These additional site trend reports will be presented in SQRT and incorporated in the APRRs to identify any corrective actions needed. A plan for implementing these additional reports (data collection method, procedures, etc.) will be developed and implemented thereafter.	15-Jul-17	14-Jul-17	Complaints		
FDA Inspection	6	Evaluate SOP-DVL-PRT-00002 procedure for potential updates to include the development of a system level reliability and to ensure linkage to the design outputs. The procedure will be applied to (b) (4) products. The procedure will require the Design Input document, PRD/TRD, to include cross reference to the risk assessment and documentation supporting the individual design inputs. Training methodology using human performance tools will be developed to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6, 7, 8	Risk Management file will be updated with a risk assessment performed by a CFT including representatives from Safety/Medical/Clinical groups, to document essential attributes and their criticality and rationale for design inputs. Risk Management file will be updated with a risk assessment including representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality/severity based on the emergency, life-saving intended use of the product. The risk management file will be updated with a risk assessment including review by representatives from Safety/Medical/Clinical to document the rationale for the ranges of the essential performance inputs and their criticality based on the emergency, life-saving intended use of the product. Risk Management file will be updated with a risk assessment (states CFT (S/M/C) will be completed JUL2017) The risk management file will be updated with a risk assessment.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate potential foreseeable sequential preconditioning of auto-injectors to include in reliability testing. System level reliability risk assessment will be completed	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	MMT will evaluate its design input procedures for potential updates to include development of system level reliability.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	The design inputs document will be updated for consistency between the product requirements section and the technical requirements section.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	Risk Management file will be updated with a risk assessment performed by a cross-functional team, including Safety/Medical, to confirm essential attributes and their criticality based on severity of harm and intended use of the combination product. The PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are written in a non-conflicting or ambiguous way.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	6	PRD/TRD 16-001 rev 1, design inputs document, will be updated to include the system level reliability specification of (b) (4) %	31-Aug-17	29-Aug-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6, 7	The PRD/TRD design input document will be updated to include cross reference to the risk assessment and documentation supporting the risk assessment conclusions. PRD/TRD design inputs document will be reviewed to ensure completeness and that the inputs are not written in a conflicting or ambiguous manner. MMT will update the PRD/TRD to trace the requirements to appropriate justifications and risk assessment. The design inputs document format will be revised to eliminate ambiguity between "Must" and "Want" design inputs. The "Wants" requirements of a PRD/TRD document will be removed from the document prior to finalizing design outputs such that design outputs can be traced directly to design in/out requirements. PRD/TRD 16-001 Rev1, injection through clothing is a requirement included as part of the use specification. This will be added to the Technical Requirement of the PRD/TRD design input document MMT will review the PRD/TRD, design inputs document, to ensure completeness and that the inputs and outputs are not written in a conflicting or ambiguous manner.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	6	CFT (S/M/C) risk assessment completion. Risk control within the supply chain control plan will be evaluated to verify it supports the recommended system level reliability	31-Dec-17	28-Dec-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	6, 7	For those essential characteristics that are confirmed as critical in Table 2 of Response 6A, or modified per the safety/medical risk assessment, (b) (4) [redacted] e specification based on acceptable use for all EpiPen products including the proposed (b) (4) . For those essential attributes that are confirmed critical through the risk assessment process, a (b) (4) specification, based on acceptable use For those essential functional attributes as described in Table 2, part 6A a (b) (4) specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability. For those essential functional attributes as described in Table 2, part 6A a (b) (4) specification based on User/Patient needs will be reassessed to determine an appropriate AQL or quality standard that sets a test sample size commensurate with demonstrating system level reliability. These values will be applied to all relevant documents and the necessary updates will be made.	31-Dec-18		Design Controls		
FDA Inspection	7, 8	MMT will take the preventative action to evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated as required to include a cross reference of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the updated procedure. Evaluate SOP-DVL-PRT-00003 for linking design outputs to the design input requirements and the procedure will be updated to include evaluations of design output conformance to design inputs. Training methodology using human performance tools will be used to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	7	Design outputs will be reviewed to ensure completeness	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	7, 8	As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4) % for essential performance requirements and reasonably foreseeable sequential pre-conditioning. This will be documented as a design output, in the engineering drawings: (b) (4) [redacted] As part of our corrective action the design inputs requirements of PRD/TRD 16-001 Rev 1 will be updated to include the system level reliability requirement of (b) (4) % for essential performance requirements and reasonably foreseeable sequential pre-conditioning. This will be documented as a design output, in the engineering drawings: (b) (4) [redacted] Reliability will then be defined in the design output and used to determine design verification requirements.	31-Aug-17	31-Aug-17	Design Controls		
FDA Inspection	8	Evaluate the design verification and validation procedure SOP-DVL-PRT-00004 for linking design verification requirements to the design input and output requirements. The procedure will be updated and training methodology using human performance tools will be used to assure adherence with the procedure	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Evaluate the design control procedures for needed updates to ensure linkage of design verification requirements to the design input and outputs. Training methodology using human performance tools will be used to assure adherence with the procedure.	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Design Control Procedures will be updated to require evaluation of foreseeable sequential conditioning	31-Jul-17	28-Jul-17	Design Controls		
FDA Inspection	8	Design inputs and outputs will be reviewed to ensure completeness.	31-Jul-17	28-Jul-17	Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	8	MMT will develop through the risk assessment process the foreseeable sequence of conditioning requirements for design verification and commercial process validation functional testing to be included as a component of the design verification and design validation plans. PRD/TRD 16-001 Rev 1 will be updated to include requirements for foreseeable sequential testing.	31-Aug-17	29-Aug-17	Design Controls		
FDA Inspection	8	Execute a study with full functional system level reliability testing (for epinephrine bitartrate) including sequential foreseeable preconditioning of auto-injectors, if required, [redacted] require functional system level reliability testing of the auto-injector device at end of product expiry, [redacted] stability for future submission lots. For submissions made [redacted]) may be included.	30-Sep-17	29-Sep-17	Design Controls		
FDA Inspection	9	Basic unit dFMEA will be approved.	31-May-17	25-May-17	Design Controls		
FDA Inspection	9	Basic unit dFMEA will be [redacted]	31-Aug-17	31-Aug-17	Design Controls		
FDA Inspection	9	dFMEA risk assessment will be incorporated into the plant quality systems including QTS, Complaints, Change Control and for risk management.	15-Nov-17	15-Nov-17	Quality Systems		
FDA Inspection	9	The dFMEA reference [redacted] will be reviewed at a minimum of annually as part of the APRR	28-Feb-18	19-Oct-17	Quality Systems		
FDA Inspection	10	A new procedure to address preventive maintenance for the [redacted] the auto-injectors (SOP-QLC-SQC-11108)	30-Apr-17	28-Apr-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394 will be revised by April 30, 2017 to (b) (4) SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be (b) (4) performance of the test	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	Preventative maintenance procedures for all other equipment in the lab will be confirmed	30-Apr-17	28-Apr-17	Laboratory		
FDA Inspection	10	A (b) (4) . Action items will be established if any statistical differences are identified.	15-May-17	15-May-17	Operational Excellence		
FDA Inspection	10	A FMEA will be completed to identify and prioritize potential failure modes in the functional lot release test procedures and testing process. A plan to implement mitigating actions for any failure modes with unacceptable risk priority numbers.	15-Jun-17	15-Jun-17	Laboratory		
FDA Inspection	10	A process has been developed for the (b) (4) Administrators to prompt and follow up with managers to create/modify curricula for new employees, new contingent staff or staff with job assignment changes. This process is already in place, but will be formally defined in a new (b) (4) SOP.	30-Jun-17	30-Jun-17	Quality Systems		
FDA Inspection	10	New (b) (4)	15-Jul-17	15-Jul-17	Laboratory		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	10	SOP-QLC-SQC-00307 and SOP-QLC-SQC-00394, will be enhanced to provide specific instructions for the (b) (4) (b) (4) will be added the SOPs to ensure (b) (4) The additional detail will describe what types of (b) (4) .	31-Jul-17	28-Jul-17	Laboratory		
FDA Inspection	10	MMT curricula and curricula assignments for all colleagues will be reviewed by the responsible area manager or their designee to ensure assignments are correct and complete. This will be facilitated by Training Systems and area training staff and formally documented according to SOP-TRN-GEN-00044, curricula reviews will be completed (b) (4) thereafter.	31-Aug-17	31-Aug-17	Quality Systems		
FDA Inspection	10	MMT will evaluate the potential to (b) (4) . This would (b) (4)	30-Sep-17	29-Sep-17	Laboratory		
FDA Inspection	11	SOP-LAB-MIC-00416 will be revised to also include this same holistic review of all lots that could be in scope of a sterility test failure, in accordance with SOP-QLA-MQA-00720	30-Jun-17	08-Jun-17	Laboratory		
FDA Inspection	12	Awareness training will be performed to (b) (4) This activity will be covered by all (b) (4) and will take place prior to (b) (4)	30-Apr-17	26-Apr-17	Aseptic Operations		
FDA Inspection	12	(b) (4) (b) (4) . These tools will better facilitate the (b) (4) .	15-Jun-17	08-Jun-17	Aseptic Operations		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	12	(b) (4) The (b) (4) in this area of the filling process will enhance (b) (4) and reduce potential for human intervention during the (b) (4) project's comprehensive validation.	15-Jun-17	14-Jun-17	Aseptic Operations		
FDA Inspection	12	(b) (4) the mid-June (b) (4) implementation. Applicable site personnel will train on this documentation update and the action will be added to the aseptic training program	15-Jun-17	13-Jun-17	Aseptic Operations		
FDA Inspection	12	Methods for (b) (4) by the corporate Microbial and Aseptic Support group	15-Jun-17	15-Jun-17	Laboratory		
FDA Inspection	12	An (b) (4) will be developed by July 1, 2017 as needed based on the findings of the evaluation	01-Jul-17	30-Jun17	Aseptic Operations		
FDA Inspection	12	A (b) (4) on the (b) (4) The (b) (4) in this area of the filling process will enhance (b) (4) and reduce potential for human intervention during the (b) (4) project's comprehensive validation.	20-Jul-17	19-Jul-17	Validation		
FDA Inspection	12	New production procedure will be created to include examples in which (b) (4)	20-Sep-17	28-Aug-17	Aseptic Operations		
FDA Inspection	12	SOP-QLA-VAL-00020 will be revised to require each (b) (4) media fill to produce a (b) (4)	31-Oct-17	05-Sep-17	Validation		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	12	MMT will engage SME's within Industry network with expertise in the design of (b) (4) to evaluate whether (b) (4) to reduce the risk of contamination during intervention (b) (4) and all other interventions performed on the (b) (4).	31-Dec-17	31-Dec-17	Aseptic Operations		
FDA Inspection	12	Based on the conclusions of the evaluation (b) (4)), an action plan will be developed by January 31, 2018 to implement equipment modifications or other recommendations made by the expert.	31-Jan-18		Aseptic Operations		
FDA Inspection	13	Current instructions on (b) (4) will be clarified to (b) (4) OP-MAN-INS-10154, RM-MAN-INS-10153, RM-MAN-INS-10152 and RM-MAN-PKG-10159 will be updated to include these instructions	15-May-17	15-May-17	Packaging & Inspection		
FDA Inspection	13	A (b) (4) will be performed. The (b) (4) During the (b) (4) will represent worse case conditions. Results from the (b) (4) will be compared to determine if any additional (b) (4) should be implemented	30-Jun-17	29-Jun-17	Validation		
FDA Inspection	13	SOP-QLA-GEN-00802 will be revised to define requirements and provide examples for when to perform change effectiveness checks and risk assessments, specifically, for (b) (4)	31-Aug-17	30-May-17	Validation		
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to (b) (4) of the complete manufacturing process) – EpiPen	15-Dec-17 Revised: 02-Mar-18		Validation		
FDA Inspection	13	Full process validation from formulation through labeling of the assembled units will be completed (to establish a (b) (4) of the complete manufacturing process) - ATNAA/DuoDote	29-Jun-18		Validation		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	n/a verbal	Update the MMT complaint SOP to (b) (4) complaint type based upon a review of historical complaint rates. Implement similar complaint rate signal limits for all expedited complaint types.	31-May-17	31-May-17	Complaints		
FDA Inspection	n/a verbal	Update Annual Product Records Review procedure SOP-QLA-MQA-00710 to include sections on: 1. Trending, tracking and (b) (4) for product defects 2. (b) (4) Analysis	31-May-17	31-May-17	Quality Systems		
FDA Inspection	n/a verbal	Change acceptance criteria in the final product release batch records to require (b) (4) average specification for (b) (4) .	31-May-17	25-May-17	Laboratory		
FDA Inspection	n/a verbal	Automated vision systems for 100% inspection of the power pak (b) (4)	20-Sep-17	20-Sep-17	Quality Systems		

Table III **CAP Related Corrective and Preventative Action Tracking as a Resulting from work completed under 483 commitments (by order of Due Date)**

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)						
CAP							
CAP							
CAP							
CAP							
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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)						
CAP							
CAP							
CAP							
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Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)						
CAP							
CAP							
CAP							
CAP							
CAP							
CAP							
CAP							

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)						
CAP							
CAP							

Table IV FDA Warning Letter Related Corrective and Preventative Action Tracking, by order of Observation and Due Date

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Drug CGMPs							
FDA Inspection	1	JA-DLV-PDV-10803 job aid will be updated to include specific detail on examining the safety release component related to this type of complaint by October 6, 2017.	06-Oct-17	06-Oct-17	Complaints		
FDA Inspection	1	Create a plan to conduct a similar (to that of SCAR) retrospective review, under protocol, of other failures or discrepancies that did not result in manufacturing investigations, such as [redacted (b) (4)] for in-coming or finished goods.	31-Oct-17	31-Oct-17	Quality Systems		
FDA Inspection	1	Conduct a comprehensive retrospective review of the manufacturing investigations for the site's other marketed products, pursuant to similar protocols. Significant findings from the retrospective reviews will be included in future quarterly updates to FDA.	01-Nov-17	01-Nov-17	Quality Systems		
FDA Inspection	1	Evaluate potential changes to the device to eliminate this use-related error regarding the safe pin.	15-Nov-17	15-Nov-17	Design Controls		
FDA Inspection	1	Contract a third-party cGMP consultant to conduct batch record review for EpiPen batches, which will include a review of associated investigations, for [redacted (b) (4)].	30-Nov-17	30-Nov-17	Quality Systems		
FDA Inspection	1	SOP-QLC-QLE-00702, Product Complaint Handling, will be updated to include requirement for a formal risk assessment to assure that all potential patient hazards are considered as part of the root cause analysis and identified corrective actions.	30-Nov-17	30-Nov-17	Complaints		
FDA Inspection	1	SOP-QLA-MQA-00720, Event and Deviation Reporting (ER&QAR) will be updated to require that manufacturing investigations will be formally evaluated for their potential to impact patient use and safety as well as product quality. If the initial assessment concludes that there is potential impact to the device or device constituents, [redacted (b) (4)].	30-Nov-17	30-Nov-17	Quality Systems		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	1	MMT will assess additional opportunities to enrich the current process for incorporating review of relevant adverse event data in conjunction with our pharmacovigilance team. This will be incorporated into existing MMT Site Quality Review Team ("SQRT") meetings and quality meetings that take place jointly with the pharmacovigilance team on a [redacted (b) (4)].	30-Nov-17	30-Nov-17	Quality Systems		
FDA Inspection	1	Fill a new leadership role within the quality organization, Combination Product Program Director, to oversee quality and compliance including: Design Controls, Purchasing Controls and Quality Risk Management. This role has been posted and active recruitment is in progress.	31-Jan-18	23-Oct-17	Design Controls		
FDA Inspection	1	Execute protocol for failures or discrepancies that did not result in MIR for in-coming or finished goods.	31-Mar-18		Quality Systems		
FDA Inspection	1	Enhance the existing training program, with an emphasis on combination products and device requirements. The program will be developed with input from a third-party cGMP consultant.	31-Oct-18		Quality Systems		
FDA Inspection	1	MMT will establish an [redacted (b) (4)]	31-Oct-18		Quality Systems		
FDA Inspection	1	Assess need for continuing [redacted (b) (4)] which includes a review of associated investigations.	01-Nov-18		Quality Systems		
FDA Inspection	2	Form a cross-functional Complaints Analysis Trend Team. This team will analyze complaint trend data, support trend investigations including identification of CAPA and further refine complaint trend data presentation and statistical analysis.	01-Nov-17	01-Nov-17	Complaints		
FDA Inspection	2	GPB-QS1073, Prioritization of Pfizer Product Quality Complaint will be revised include EpiPen specific prioritization information in line with the Complaint Prioritization Protocol.	06-Nov-17	06-Nov-17	Complaints		
FDA Inspection	2	SOP-QLC-QLE-00702, Product Complaint Handling, will be revised to ensure that complaint investigation testing and techniques also consider potential patient risk and escalation where appropriate. Establish a link between the complaint trending process and review of the risk management file.	30-Nov-17	30-Nov-17	Complaints		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	SOP-QLC-QLE-00702, Product Complaint Handling will be revised to provide guidance to Complaint Investigators on verifying/assigning complaint subclasses to ensure consistent classification in support of accurate trending.	30-Nov-17	30-Nov-17	Complaints		
FDA Inspection	2	Conduct a retrospective assessment of all complaints received (b) (4) [redacted] that would now be classified as (b) (4) [redacted]	30-Jan-18		Complaints		
Device QSR Requirements							
FDA Inspection	N/A	Conduct a comprehensive assessment of quality systems against the QSR with oversight and input from a third-party cGMP consultant.	31-Oct-17	30-Sep-17	Quality Systems		
FDA Inspection	1	Review supplier Quality Agreements for critical components identified in the dFMEA and work with these suppliers to develop appropriate control strategies for the identified high-risk components. These strategies may include the trending of critical quality attributes and a periodic review of supplier process capabilities by the SQRT.	01-Mar-18		Quality Systems		
FDA Inspection	2	Provide a plan for a detailed timeline for EpiPen design verification based on product lifecycle design assessments.	31-Oct-17	31-Oct-17	Design Controls		
FDA Inspection	2	Revise design verification procedure SOP-DVL-PRT-00004, Design Verification and Validation for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction, to reflect enhanced process and documentation in Design History File.	30-Nov-17	30-Nov-17	Design Controls		
FDA Inspection	2	EpiPen Design Verification - Review and Update Design Inputs	28-Feb-18		Design Controls		
FDA Inspection	2	To ensure alignment of design outputs to design inputs and design verification acceptability, MMT will execute a Design Traceability Matrix based on the requirements contained in SOP-DVL-PRT-00003, Design Outputs for New Products, Major Changes to Existing Products and Changes Affecting Product/ User Interaction	31-Oct-18		Design Controls		
FDA Inspection	2	Approve final report of design verification, including sequential preconditioning, for the EpiPen NGA Auto-Injector. (b) (4) [redacted]	31-Dec-18		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	2	Approve final report of design verification, including sequential preconditioning, for the EpiPen NGA Auto-Injector. (b) (4)	31-Jul-20		Design Controls		
FDA Inspection	3	SOP-DVL-PRT-00004, Design Verification and Validation for New Products, Major Changes to Existing Products and Changes Affecting Product/User Interaction will be updated to include all required design validation elements for combination products and to set forth the process for conducting design validation	30-Nov-17	30-Nov-17	Design Controls		
FDA Inspection	3	Develop a schedule for completing the activities for design verification for other approved products	30-Nov-17	30-Nov-17	Design Controls		
FDA Inspection	3	For EpiPen products: Comprehensive review of user needs	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Update risk analyses as appropriate	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Performing human factors formative studies as applicable	28-Feb-18		Design Controls		
FDA Inspection	3	For EpiPen products: Submit a human factors summative validation protocol, for review by the Agency	31-Mar-18		Design Controls		
FDA Inspection	3	Perform a pFMEA and integrate it into the site's overall risk management process.	31-Mar-18		Design Controls		
FDA Inspection	3	For EpiPen products: Execute the summative validation protocol	31-Oct-18		Design Controls		
FDA Inspection	3	For EpiPen products: Submit an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	31-Jan-19		Design Controls		
Quality Agreements							
FDA Inspection	N/A	As an improvement, MMT commits to conduct an assessment of its QA with Mylan by October 31, 2017. The goal of the assessment will be to identify opportunities to expand the current QA to improve express alignment with both QSR requirements and drug cGMP regulations.	31-Oct-17	31-Oct-17	Quality Systems		

Table V CAP Related Corrective and Preventative Action Tracking as a Resulting from work completed under FDA Warning Letter commitments by order of Observation and Due Date

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Drug Regulations							
FDA Inspection	Result of Obs. 1	Retrospective review of failures or discrepancies that did not result in MIR. - Protocol for Epinephrine products	15-Dec-17	15-Dec-17	Quality Systems		
FDA Inspection	Result of Obs. 1	Retrospective review of failures or discrepancies that did not result in MIR. - Protocol for other products (non-Epinephrine product)	15-Jan-18		Quality Systems		
FDA Inspection	Result of Obs. 1	Retrospective review of the manufacturing investigations for the site's other marketed products. Significant findings from the retrospective reviews will be included in future quarterly updates to FDA.	01-Feb-18		Quality Systems		
FDA Inspection	Result of Obs. 1	Retrospective review of failures or discrepancies that did not result in MIR. - Final Report Epinephrine Product	28-Feb-18		Quality Systems		
FDA Inspection	Result of Obs. 1	Retrospective review of failures or discrepancies that did not result in MIR. - Final Reports for Other Products	30-Apr-18		Quality Systems		
FDA Inspection	Result of Obs. 1	Conduct Engineering Evaluations/Studies to Select short and/or Long Term Solutions to Eliminate Spontaneous Activation	31-Jul-18		Design Controls		
Device QSR Requirements							
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Comprehensive Review of User Needs	30-Jun-18		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Update Risk Analyses as appropriate	31-Oct-18		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Comprehensive Review of User Needs	31-Dec-18		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Performing human factors formative studies as applicable	31-Dec-18		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	31-Jan-19		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Update Risk Analyses as appropriate	30-Apr-19		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Performing human factors formative studies as applicable	30-Jun-19		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	31-Jul-19		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Execution of the summative validation protocol.	31-Dec-19		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Comprehensive Review of User Needs	28-Feb-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - DuoDote Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	28-Feb-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Execution of the summative validation protocol.	31-May-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Comprehensive Review of User Needs	30-Jun-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Update Risk Analyses as appropriate	31-Jul-20		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Result of Obs. 3	Remediation - ATNAA Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	31-Aug-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Performing human factors formative studies as applicable	30-Sep-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	31-Oct-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Update Risk Analyses as appropriate	31-Oct-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Performing human factors formative studies as applicable	31-Dec-20		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Execution of the summative validation protocol.	31-Jan-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	31-Jan-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Comprehensive Review of User Needs	31-May-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Execution of the summative validation protocol.	31-May-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - AtroPen Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	31-Aug-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Update Risk Analyses as appropriate	30-Sep-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Performing human factors formative studies as applicable	30-Nov-21		Design Controls		

Commitment Type	Observation Number	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
FDA Inspection	Result of Obs. 3	Remediation - Morphine Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors	30-Nov-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Comprehensive Review of User Needs	30-Nov-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	31-Dec-21		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Update Risk Analyses as appropriate	31-Mar-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Execution of the summative validation protocol.	30-Apr-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Performing human factors formative studies as applicable Deliverable: Approved studies Report	31-May-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Submitting a human factors summative validation protocol, for review by the Agency	30-Jun-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Diazepam CANA Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	31-Oct-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Execution of the summative validation protocol.	31-Oct-22		Design Controls		
FDA Inspection	Result of Obs. 3	Remediation - Pralidoxime Chloride Auto-Injector - Submitting an overall design validation summary report including an HFE/UE report summarizing all human factors and usability engineering work including the human factors validation study	30-Apr-23		Design Controls		

Table VI **CAP Related Corrective and Preventative Action Tracking as a Result of 3rd Party Phase I Assessments (by order of Due Date)**

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Compliance Action Plan – Design Controls Assessment & Statistical Methods Assessment						
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						
CAP						

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Compliance Action Plan – Product Complaint System Assessment						
CAP	(b) (4)					
CAP						
CAP						
Compliance Action Plan – Investigation Systems Assessment						
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Compliance Action Plan – Corrective Actions and Preventative Actions Systems Assessment						
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						
Compliance Action Plan – Management Controls Assessment						
CAP	(b) (4)					
CAP						
CAP						

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
CAP	(b) (4)					
CAP						
Compliance Action Plan – Purchasing Controls Assessment						
CAP	(b) (4)					
CAP						

Table VII **CAP Related Corrective and Preventative Action Tracking as a Result of November 09, 2017 Regulatory meeting (by order of Due Date)**

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
Compliance Action Plan – November 2017 Regulatory Meeting						
CAP	(b) (4)					
CAP						
CAP						
CAP						
CAP						
CAP						

Commitment Type	Task Name	Target Completion Date	Actual Completion Date	Work-stream	CAPA Effectiveness Check Completion Date	CAPA Effectiveness Results
	(b) (4)					

Table VIII Corrections to CAP document (by Table and table order)

Table #	Task Name	Change from previous CAP version	Rationale
Table I	(b) (4)		
Table II			
Table II			

Table #	Task Name	Change from previous CAP version	Rationale
Table IV	(b) (4)		
Table VI			